## REMARKS

I. Introduction

It is respectfully requested that this Amendment After Final Rejection be entered and made of record. It is believed that the following amendments and remarks place the application in a form for allowance. The following amendments and remarks at least place the claims in a better form for appeal. No new matter is presented, as such the amendment is proper under 37 C.F.R. § 1.116.

Claims 1, 2, 4-9, 11-14, 16, 19, 21-29, and 32-33 remain in the case. Claims 30-31 and 34 have been canceled.

II. Claim Rejections - 35 U.S.C. § 112, First Paragraph

Claims 1-2, 4-9, 11-14, 16, 19, and 21-34 were rejected under 35 U.S.C. § 112, first paragraph. The Examiner states that the complex of the claims should be further limited so as to express the unique physical structure of Applicant's PVAP-PVP complex which has been prepared in the instant specification. The Examiner notes that the limitations of claims 31 and 34 express the complex structure of the claimed complex.

Applicant has now amended the composition claims to include the spectrum bands set forth in claims 31 and 34, now canceled. It is therefore believed that the composition claims now sufficiently define the unique physical structure of the PVAP-PVP complex. Applicant therefore respectfully requests that this ground of rejection be withdrawn, at least with respect to the composition claims.

With respect to the method claims, they have now been amended to more precisely define the steps of making Applicant's polymer entrapped drug, including the steps of:

(1) combining PVAP and PVP in a non-acidic medium selected from the group consisting of an aqueous alkaline solution or an organic solvent to form a PVAP-PVP complex;

(2) adding a drug to the aqueous alkaline solution or the organic solvent prior to the formation of the PVAP-PVP complex; and

(3) adjusting the pH of the mixture to an acidic pH to form drug granules entrapped in the PVAP/PVP complex.

It is respectfully submitted that Applicant's claimed process inherently and necessarily produces the PVAP-PVP complex with its unique physical structure. Thus, the addition of the structural features in Applicant's claims would be redundant. Applicant therefore respectfully requests that this ground of rejection also be withdrawn with respect to the method claims.

III. Claim Rejections - 35 U.S.C. § 103(a)

Claims 19, 21-30, and 32 were rejected under 35 U.S.C. § 103(a) as being obvious over Gupta et al. Drug Development and Industrial Pharmacy (1994) or M.A. Elegakey et al. P.P.S. 434-440 or Takayana Chem. Pharm. Bull. PPS 3921-4926. The Examiner argues that a free carboxylic group containing polymer and drug PVP complex of the claims may be equivalent to the drug complexes of the references of the same chemical formula. The Examiner further notes that the claims are not limited to complexes of different physical structure and properties than are possessed by compositions of the cited prior art wherein a carboxylic copolymer and PVP entraps an active agent such as ibuprofen, and that release properties of the entrapped drug complexes of the instant claims may be the same as these properties found in the prior art. Applicant respectfully traverses this rejection.

Gupta, Elegakey, and Takayana all describe means for producing interpolymer complexes wherein two water soluble polymers are combined to produce a complex. For instance, Gupta describes interpolymer complexation of Carbopol-934 with polyvinyl pyrrolidone and hydroxypropyl cellulose, all water soluble polymers. (p. 315). Further, Elegakey teaches the preparation of PVP-Carbopol complexes using a flocculation process. The flocculation process involves placing the carbopol in aqueous medium, then mixing in the PVP. (See Elegakey article in Sci. Pharm, p. 429). Finally, Takayama describes interpolymer complex formation of PVP with CP-II (Carbopol 934). (Pages 4922-4923).

In comparison, Applicant's claimed complex, unlike the cited prior art, involves the complexation of PVP with the non-water soluble polymer PVAP. PVAP is chemically very different from the polymers described in the cited references since PVAP structurally includes a carboxylic group that is part of a phenyl ring which in turn is attached to the polymer backbone, while the cited references involve the use of polymers having a free carboxylic group attached directly to the polymer backbone. This unique chemical structure renders PVAP practically insoluble in water.

The PVAP polymer of Applicant's invention further differs from those of the cited art in that it is practically insoluble in acidic conditions. PVAP has been used as an enteric polymer, meaning that the polymer remains intact (insoluble) in the acidic environment of the stomach, but dissolves in the more alkaline pH of the intestine ($\approx$ 7.4). In contrast, the polymers of the cited art remain soluble in acidic conditions.

It is respectfully submitted that a person skilled in the art at the time of Applicant's invention would not have been inclined to manufacture Applicant's PVP/PVAP complex in view of the teachings of the cited references since the references teach only the use of water-soluble

carboxylic polymers. In fact, the cited references actually teach away from Applicant's PVAP/PVP complexation process that must take place at a non-acidic pH. It is therefore submitted that claims 19, 21-30, and 32 are patentably distinguished by Gupta or Elegakey or Takayana, and Applicant therefore respectfully requests that this ground of rejection be withdrawn.

IV. Conclusion

It is believed the application is in a prima facie condition for allowance. Allowance is respectfully requested.

No fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Respectfully submitted,

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**AMENDMENT — VERSION WITH MARKINGS TO SHOW CHANGES MADE — DO NOT FILE**

**In the Claims**

Claims 1, 8, 19, 23-25, 30, and 31-34 were amended as follows:

1. (Twice Amended)

A polymer complex for entrapping drug granules comprising:

a complex of polyvinyl acetate phthlate (PVAP); and

polyvinylpyrrolidine (PVP);

said PVAP-PVP complex having bands at about 1657 $cm^{-1}$ and 1724 $cm^{-1}$ in the spectrum of the PVAP-PVP complex.

8. (Twice Amended)

A polymer-entrapped drug comprising:

a drug that is insoluble in organic solvent, but soluble or suspendable in an alkaline solution and insoluble in aqueous acidic solutions;

a complex of polyvinyl acetate phthlate (PVAP); and

polyvinylpyrrolidine (PVP);

said PVAP-PVP complex having bands at about 1657 $cm^{-1}$ and 1724 $cm^{-1}$ in the spectrum of the PVAP-PVP complex.

19. (Twice Amended)

A method of making a polymer entrapped drug comprising the steps of:

combining polyvinyl acetate phthlate (PVAP) and polyvinylpyrrolidine (PVP) [at least one polymer having at least one free carboxyl group and a drug] in a non-acidic medium selected from the group consisting of an aqueous alkaline solution [or] and an organic solvent to form a [mixture] PVAP-PVP complex,

adding a drug to the aqueous alkaline solution or the organic solvent prior to the formation of the PVAP-PVP complex, said drug being insoluble in the organic solvent, but soluble or suspendable in an alkaline solution and insoluble in aqueous acidic solutions; and

adjusting the pH of the mixture to an acidic pH to form [entrapped] drug granules entrapped in the PVAP/PVP complex.

23. (Amended)

A method according to claim 19 wherein the pH of the aqueous alkaline mixture containing drug and [polymers] PVAP/PVP complex is lowered to an acidic pH of less than about 4.

24. (Amended)

A method according to claim 23 wherein the pH of the aqueous alkaline mixture containing drug and [polymers] PVAP/PVP complex is lowered to a pH of about 3 or below.

25. (Amended)

A method according to claim 19 wherein the pH of the aqueous alkaline mixture containing drug and [polymers] PVAP/PVP complex is lowered with hydrochloric acid.

Claims 30 and 31 have been canceled.

32. (Amended)

A polymer complex for entrapping drug granules formed by the process of:

combining polyvinyl acetate phthlate (PVAP) and polyvinylpyrrolidine (PVP) [at least one polymer having at least one free carboxyl group and a drug] in a non-acidic medium selected from the group consisting of an aqueous alkaline solution [or] and an organic solvent to form a [mixture] PVAP-PVP complex,

adding a drug to the aqueous alkaline solution or the organic solvent prior to the formation of the PVAP-PVP complex, said drug being insoluble in the organic solvent, but soluble or suspendable in an alkaline solution and insoluble in aqueous acidic solutions; and

adjusting the pH of the mixture to an acidic pH to form [entrapped] drug granules entrapped in the PVAP/PVP complex.

14 ~~33~~. (Amended)

A polymer-entrapped drug comprising:

a drug that is insoluble in organic solvent, but soluble or suspendable in an alkaline solution and insoluble in aqueous acidic solutions;

said drug being entrapped in a complex of polyvinyl acetate phthlate (PVAP) and polyvinylpyrrolidine (PVP);

said PVAP-PVP complex having bands at about 1657 $cm^{-1}$ and 1724 $cm^{-1}$ in the spectrum of the PVAP-PVP complex.

Claim 34 has been canceled.